I. BACKGROUND

1. Hello, my name is Dr. Cheryl Blume. As you have heard, I am the President of Pharmaceutical Development Group. It is a consulting firm that specializes in drug development and helps drug companies get their drugs reviewed and approved by the U.S. Food & Drug Administration.

2. I have been asked to investigate and provide opinions about whether Warner Lambert and Pfizer failed to warn doctors and patients about the risks of suicidal behavior with Neurontin use and whether Neurontin can cause suicidal behavior in people who take it. My opinion on both questions is YES: First, it is my opinion that the Defendants failed to warn doctors and patients about suicidality with Neurontin and, second, Neurontin does cause suicidal behavior. My opinions in this case are given with a reasonable degree of scientific certainty. In this statement, I will go into detail about the evidence concerning my opinions in the areas that Mr. Lanier told you about in his opening statement, including the following areas:

   A. Only FDA approved uses can be advertised.
   B. Neurontin is an epilepsy drug.
   C. Neurontin is only approved for limited pain use.
   D. Neurontin was never approved for Richard Smith's type of pain: general neuropathic pain.
   E. Neurontin has significant effects.
   F. Neurontin increases the risk of suicide.
   G. Pfizer ignored red flags.
   H. Pfizer failed to warn.

3. I cannot stress enough that the Defendants did not need to have definitive proof that Neurontin causes suicidal behavior before warning doctors and patients about it. The rules require that a label be changed when there is reasonable evidence of a relationship -- not definitive proof. Based upon my review of the available information, certainly no later than 2000, the company had adequate information to substantially enhance their warnings about the potential of suicidal behavior.

4. It is important that I tell you that the Smith family's attorneys have paid my company for our time and work. Over the past 7 years, these fees have been approximately 5% of the company's total income. My company's work with Neurontin has taken hundreds and hundreds of hours and has involved the review of extensive volumes of documents and data. I also reviewed over one hundred of Defendants' confidential research studies. Because of my thorough review of the documents and data produced by Defendants in this case, I am able to reach opinions that are reasonable and scientific. My opinions are based upon many things, including my review of Defendants' confidential research with animal studies and clinical trials involving thousands of patients, their Drug Applications to the FDA, published medical literature, and side effects --- what we call adverse events --- that were reported with the use of Neurontin. I have also reviewed deposition transcripts and exhibits disclosed during this lawsuit.

5. You may wonder where I received all this information. Much of the information came to me from the Defendants' own confidential documents. The Defendants' lawyers gave it to the Smith's attorneys, and then those attorneys gave it to me on a computer drive that had

millions of pages of documents. To be able to speak to you today, I reviewed a great deal of those documents. My company performed searches through the documents and collected materials that formed the basis of my opinons. We also performed extensive independent research through the medical literature and other available regulatory documents. I have worked closely with the plaintiffs' attorneys in reviewing the documents and data. In particular, I have worked with one of the plaintiff's attorneys, Keith Altman, who assisted in putting together charts of the data that was available for me to review.

6. It is also important for me to tell you that what I did here is the same tasks that I provide to drug companies outside of litigation. I used the very same methods as I have been using for the past 25 years. My company's litigation related activities represent approximately 20-30% of the work that my company does. For the remainder of our work, my company is responsible for the review of similar data and information and in the preparation of submissions to the FDA.

7. My participation in this lawsuit has included providing the attorneys with an expert report of over 200 pages that detailed my opinions. Obviously, the statement that I am reading to you now can only summarize my findings in this case. I have also given testimony during depositions and in court for this case, very much like I am doing right now.

8. In this case, Warner Lambert and Pfizer failed to respond to "safety-signals" or what I call "red flags" regarding the dangers with Neurontin, particularly with people who were taking Neurontin for "off-label" uses, like Mr. Smith.

II. SAFETY AND REGULATORY OVERVIEW

A. Only FDA approved uses can be advertised

9. Now in order to get to my opinion, let me give you some background about how drugs get approved for sale in this country. You see, before a new drug can be marketed in the United States, a drug company has to submit a new drug application to the FDA. The application includes the results of animal studies and clinical trials. The drug company must show that the drug is safe and efficacious for the illness the drug is supposed to help treat. All drugs have risks, but the company must show that the benefits of the drug outweigh those risks. This is required by federal law and regulations. After the drug's approval by FDA, the drug company still has to conduct extensive safety surveillance on the drug and be aware of side effects that are reported by physicians and patients nationwide. After the drug's approval, the drug company can only advertise and promote the sale of their drug for the approved use.

Neurontin is primarily an epilepsy drug.
Neurontin is only approved for limited pain use

10. So, what does this have to do with Neurontin? Well, in this case we know that at the time Mr. Smith died, Neurontin was approved only for very limited uses. It was approved to treat epilepsy and for the treatment of post-herpetic neuralgia --- a very limited type of nerve pain, also called "shingles". Now, an approval by the FDA means that the FDA concluded that the

benefits of the drug outweigh the risks known at that time for use with epilepsy and for post-herpetic-neuralgia.

11. You may not be aware, but the FDA does not conduct independent research when approving a drug. The FDA relies upon the work undertaken by the company and presented as part of the New Drug Application (NDA). So, in this case, the only uses that the FDA approved were the uses of Neurontin for epilepsy treatment and for shingles pain.

12. As part of the NDA, the drug company tests the drug on people to see if the drug is effective and to try to see if the drug has obvious safety risks. Unfortunately, these clinical trials are often done with small numbers of people for short periods of time. As a result, there are risks that are not discovered until after the drug is approved and is being used by many people. Also, let me be very clear: just because the FDA has found the drug's benefits outweighed the risks for uses like epilepsy and shingles pain, there is no proof that FDA ever decided the drug was safe for anything else.

13. Why is this point important? Because the defendants were actually marketing and promoting Neurontin for unapproved, "off-label" uses far beyond these limited FDA approvals. Doing this placed the public at risk of being harmed, and Mr. Smith is the victim of the Defendants' actions. Even if the Defendants try to claim that they did not promote the drug improperly, they certainly knew that most of the people who were using the drug were using it for off-label uses. Since Neurontin did not have FDA approvals for these uses, the Defendants didn't know if Neurontin was safe or even effective for their unproven uses. Patients like Mr. Smith were not warned about the potential for suicide-related side effects with Neurontin.

<u>Neurontin was never approved for Richard Smith's type of pain: general neuropathic pain</u>.

14. Mr. Smith was not prescribed Neurontin for either of the approved uses. We know that Defendants knew that people were being prescribed Neurontin for "off-label" uses. As such, Defendants had an obligation to watch for safety signals and red flags --- side effects --- not only for the FDA approved uses, but also for the "off-label" uses. As I said before, the company did not have an approval for the drug for those off label uses, and they didn't know if it was safe or effective for those uses. It is my opinion that when a drug company knows that most of the people using their drug are using it for "off-label" uses, where safety and effectiveness has not been proven, then the company needs to be even more careful. After all, no benefits have been proven for off-label uses.. Based on my review of documents, Pfizer wasn't careful and people like Mr. Smith died.

15. We then ask ourselves, how were Defendants supposed to keep an eye out for these side effects? The answer is that Defendants should have established a system for pharmacovigilance activities. The World Health Organization defines pharmacovigilance as "The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem." In other words, Defendants should have "develop[ed] written procedures" (CFR 314.80(b)) for the surveillance and evaluation of psychiatric side effects, not only in the Neurontin approved uses (like epilepsy or post-herpetic neuralgia), but also for the unapproved uses (like chronic pain that Mr. Smith had). The Defendants, as I will explain later, did implement a system for collecting

information about suicidal behavior, but only after Mr. Smith died. There is no reason that this could not have been done long before his death. Essentially, Defendants did too little, too late.

16. Defendants should have tracked side effects beginning at the launch of Neurontin into the market and then throughout its entire marketing lifespan. Defendants should have closely monitored all available data, reviewed published literature, conducted necessary follow-up studies and fully explored all potential adverse events.

17. It is also critically important that Defendants should have told prescribers about these red flags in advertisements, in letters to the doctors, and when their sales people visited doctors to recommend Neurontin be used with their patients.

18. In this case with Neurontin, let me summarize for you some of the "signals" or red flags Defendants knew about but failed to warn doctors and patients.

III. RED FLAGS AND SAFETY SIGNALS

Exhibit 4712 (p.130/366)

Pfizer ignored red flags.

19. One of the strongest indicators of a relationship between a drug and an adverse event is what is called a dechallenge/rechallenge event. This is a very straightforward concept and it is critically important for pharmacovigilance. Let's say you take a drug and have a side effect. If you stopped taking the drug and the side effect goes away, that is a positive dechallenge. If you start taking the drug again and the event returns, that's a positive rechallenge. Think of it like putting up your Christmas tree. You plug in one strand of lights and it doesn't work. So you start unscrewing each bulb until all of a sudden, the strand comes on. When that bulb is taken away, the problem goes away. That is the dechallenge. Then you screw the bulb in and the lights go out again. When the bulb is added back and there is a problem again, a positive rechallenge occurs. Everyone would know that it was that one bulb that was causing the problem. A dechallenge/rechallenge event with a drug is exactly like that.

20. Take a look at this exhibit. It shows that in Defendants' clinical trials for Neurontin, their own investigators concluded that side effects of depression with Neurontin were related to the Neurontin. There was a positive dechallenge/rechallenge event. Again, let me explain. You see, when the drug company thinks that their drug is causing a side effect, they take the drug away from the patient to see what happens; this is called a dechallenge. If the side effect goes away, this is a positive dechallenge. If the drug company gives the drug back to the patient, this is called a rechallenge. During the rechallenge, if the side effect comes back, then you have a positive rechallenge. In this case with Neurontin, Defendants admit that their own investigators observed a side effect of depression and they concluded it was probably related to Neurontin. In my area, these kind of events are so rare, that even one single event like this one is a big deal. Just like the Christmas tree bulb, this is very strong evidence that the drug caused the bad effect.

Exhibit 4581 (p.101/131)

21. Now here is another red flag. In the same report, even before the person was rechallenged with the Neurontin, the Defendant drafted a confidential memo in 1990. Here, Defendants' own clinical trials reflected that Acute Severe Depression and Suicidal Ideation were expected adverse events associated with Neurontin.

Neurontin increases the risk of suicide

Exhibit 4712

22. Look at this statement from the FDA in 1992. In 1992, the FDA told Warner Lambert to watch out for depression and suicide attempts with Neurontin. FDA was concerned that depression could become worse and result in suicidal behavior.

This is what FDA said, "**[l]ess common but more serious events may limit the drug's widespread usefulness…. [D]epression, while it may [not be] an infrequent occurrence in the epileptic population, may become worse and require intervention or lead to suicide, as it has resulted in some suicide attempts.**" FDA specifically expressed concern about the side effect of "clinically important depression" and stated Neurontin's risk profile was "uncertain".

Even though the Defendants were fully aware that the drug could have these effects, the company marketed the drug "off-label" to the very individuals who were most vulnerable. Yet this very critical safety information was witheld from doctors and patients.

Neurontin has significant effects

Exhibit 4765

23. There are certain chemicals in the brain that effect how we feel. These are called neurotransmitters. You have already heard [*or will hear Plaintiff's expert*] Dr. Michael Trimble talk about these chemicals. When there is a decrease or imbalance in these brain chemicals, people can get depressed and suicidal. Now the defendants knew that Neurontin affected these chemicals. This document proves Defendants admit that neurontin affects neurotransmitters in the brain since the 1980s. This is a copy of Defendants' confidential research study from May 1984, which showed that Neurontin reduced the release of excitatory neurotransmitters like serotonin and norepinephrine. This is important because these effects could contribute to suicidal behavior. Defendants should have warned doctors about Neurontin's capacity to reduce the release of serotonin and norepinephrine in the brain. This link between neurotransmitters and depression was even admitted by Defendants' own employee and neuropharmacologist, Dr. Leslie Tive, who had responsibilities with Neurontin.

For doctors treating vulnerable patients with psychiatric and pain conditions, this is crtitical information that was not in the label. Only if a doctor specifically called the company and asked would the company tell them anything. Otherwise, it was "don't ask, don't tell" and business as usual.

Exhibit:
Deposition Testimony of Defendants' employee/neuropharmacologist
Leslie Tive, PhD

24. In this case, Defendant's employee and neuropharmacologist, Dr. Leslie Tive, has testified under oath that an imbalance in serotonin ---- either an increase or decrease ---- can be associated with depression. Lets look specifically at her deposition testimony transcript*: (read the transcript or play audio/video)*

Q. Miss Tive, do you have an understanding as to whether an increased amount of serotonin or a decreased amount of serotonin in the brain can be associated with depression?
A. An increase or decrease of serotonin in the brain can be associated with depression. But when you talk about depression, are we talking about central nervous system depression, or are we talking about clinical depression?
Q. Let's talk about clinical depression.
All right. What happens when there's a reduction in the flow of monoamines such as dopamine, serotonin, and norepinephrine?
A. You're saying monoamines in general?
Q. Correct.
A. A reduction in monoamines has been associated with depression.

Neurontin decreases serotonin and nor-epinephrine & dopamine. My opinion, like Dr. Tive, is that this is associated with depression.

Exhibit:
Brawek B., and Dooley, et al.,
Differential modulation of K+-evoked 3H-neurotransmitter release from human neocortex by gabapentin and pregabalin,
Naunyn-Schmiedeberg's Arch Pharmacol (2008).

25. Neurontin's influences on brain neurotransmitters have been reported in both animal and human studies for several years. In fact, this has been observed by Defendants' own research scientist David Dooley, in a 2008 published article, entitled "Differential modulation of K+-evoked 3H-neurotransmitter release from human neocortex by gabapentin and pregabalin". So, what this means is that they tested concentrations of GABApentin on human brain tissue, and the results were that there was a decrease in the neurotransmitter release. Again, this is

important to know because a decrease in these neurotransmitters has been associated with depression.

Pfizer ignored red flags

Exhibit 4712

26. Here is another red flag. Before Neurontin was ever approved in 1993, the Defendant's own clinical trials showed that there were 78 reports of depression (or 5.3% of the patients). There were 7 reports of depression as a serious adverse event and 9 patients withdrew from studies because of depression, some of which had suicidal ideation. It was determined that of the 78 patients reporting depression, 19 had no prior history and 22 patients required treatment for their symptoms. What this means is that 19 people who had no psychiatric problems before receiving Neurontin, later needed drug therapy for treatment of the depression triggered by Neurontin.

Exhibit 2004

27. Now in the mid-1990s, Defendants hired Dr. Michael Trimble, an expert in epilepsy drugs to review behavior side effects with Neurontin. This exhibit shows his findings. In his review of "aggression and related disorders", Dr. Trimble evaluated twenty-one (21) cases and determined that in nine (9) cases, "that behaviour problems may have been exacerbated in 4, and occurred *de novo* in 5." What this means is that the Neurontin in certain patients made their behavioral problems worse. Overall, however, these reports by Dr. Trimble, as requested by Defendants, did not consider additional psychobiological events including those related to suicidal behavior, such as suicidal thoughts and intentional overdoses. A more thorough review of psychiatric side effects should have been performed and then doctors and patients should have been warned about all possible adverse events. As I mentioned earlier, Dr. Trimble is now an expert for the Plaintiffs in this case.

Exhibit: Suicide Related Events in Safety Update Reports

28. The company received many reports of negative mood and behavioral disturbances in patients receiving Neurontin. On a periodic basis, Defendants prepared reports regarding the safety issues with Neurontin. These are called Periodic Safety Update Reports. These update reports had safety signals ---more red flags --- about neurontin and suicide related events. For example, I reviewed reports of suicide-related events for the time period of 1996-2002, all before Mr. Smith's death. You can see In Table 1, PDG provided a summary of the suicide-related events. Table 1 provides a listing of suicide-related adverse event terms found in reports. These events began to appear consistently in reports starting in 2000 and early 2001 and you can see on the chart the numbers of reports of suicide ideation (19), suicide attempt (14), and suicide (12) in the 5 years that are shown in the chart (1998-2003).

Table 1. Suicide-related Adverse Events from PSUR's

Adverse Event	1/1/97-7/31/97	8/1/97-12/31/97	2/1/99-7/31/99[#]	8/1/99-1/31/00	2/1/00-7/31/00	8/1/00-1/31/01	2/1/01-7/31/01	2/1/98-1/03[*]	Total
Intentional Overdose[&]	1	0	1	4	5	12	11	372	406

Suicide Attempt	0	0	2	2	0	2	3	14	23
Suicide Ideation	0	0	0	1	1	1	0	19	22
Suicide	1	0	0	0	1	1	1	12	16
Suicidal Thoughts	1	0	0	0	0	2	1	3	7
Suicidal	0	0	0	0	0	0	0	4	4
Suicidal Tendency	0	0	0	0	0	0	1	2	3

[#]Psychobiologic adverse events for these PSURs represent cases occurring in the United States only.
*This PSUR covers 5 years (1998-2003) and includes adverse event reports listed previously in other PSUR's.
[&]These events are not necessarily suicide attempts.

For an industry person concerned with pharmacovigilance events and drug safety, this chart is very unsettling. It shows that there are multiple events related to suicidal behavior and that these events are increasing over time. While the increase could be due to more people using the drug, it could also be due to the drug causing the effect in a vulnerable population, such as patients at increased risk for these events because of underlying diseases.

29. Take a look at this next chart. It summarizes safety related to suicide events and which should have caused Defendants to warn doctors and patients. The chart is slightly different than the chart above because it was prepared using different time and reporting conventions, but the concerns are the same. These include a 4-fold increase in suicide attempts from 1998 to 1999 and a doubling of suicide attempts from 2000 to 2001. In addition, the number of intentional overdoses showed increases from 1999 through 2002. Most critial is that despite both of these charts, the labeling wasn't changed and off-label use was skyrocketing.

Table 2. NDA Periodic Adverse Event Reports

NDA 20-235

Suicide-Related Adverse Events

Event	**10/1/96-12/31/96**	**1/1/97-12/31/97[&]**	**1/1/98-12/31/98**	**1/1/99-12/31/99**	**1/1/00-12/31/00**	**1/1/01-12/31/01**	**1/1/02-8/18/02**
Intentional Injury	**0**[#]	-	**1** (0)*	**0**	**0**	**0**	**0**
Intentional Overdose	**0**	-	**0**	**3** (3)	**23** (7)	**61** (12)	**177** (61)
Suicidal Ideation	**0**	-	**0**	**0**	**0**	**0**	**3** (3)
Suicide Attempt	**0**	-	**1** (1)	**4** (3)	**4** (4)	**8** (7)	**2** (1)
Death by Suicide	**0**	-	**0**	**0**	**0**	**0**	**1** (1)

[&] We were unable to locate this Periodic Adverse Event Report
[#] Total number of events presented in **bold** type
* coded as serious

Exhibit 5392

30. In 2001, Pfizer wanted to secure a new approval for Neurontin to treat people with certain kinds of pain. Approximately 90% of the people using Neurontin were taking it for something other than epilepsy. Many of these people were using Neurontin for pain. As I said before, since the company didn't have an approval for these other indications, it didn't know if Neurontin was safe or effective.

31. Certain people in the company decided that since they were trying to get the drug approved for pain, maybe they should look at all the people who had been using it for pain off-label. In a document from March 2001[1], the Defendants admitted that since they didn't have an approval for pain, they didn't really know if it was safe. They also admitted that Neurontin may affect these people differently than the epilepsy patients. They also admitted that people using Neurontin for "off-label" uses, such as for chronic neuropathic pain, might be more susceptible to psychiatric side effects.

32. The internal documents did not provide evidence that the Defendants ever specifically examined for off-label pharmacovigilance events.[2]

33. Given the seriousness and severity of suicide-related events, Defendants should have examined all side-effect reports from patients using Neurontin for "off-label" uses. Unfortunately, the Defendants limited their review to those side effect reports that reached a 2% threshold, so critical psychiatric adverse events were not adequately assessed.

Exhibit 4046

34. In 2002, Pfizer developed a plan to review side effects occurring at 1% or more as a threshold for a safety signal. This time they decide to search for very specific individual side effects, like "suicide attempt", or "depression", instead of using the general "psychiatric" term. This approach also excludes very specific individual terms For example, this requirement of 1% did not include the safety concern of "suicide attempts" because these events equaled only 0.24%, falling below the arbitrary threshold.

35. As part of my preparation for this case, I looked at what would have happened if the company had used a more reasonable way to look at the data. There is a standard dictionary (MedDRA) used to combine certain related adverse events. I used this to combine terms such as suicidal ideation, suicide attempt, and completed suicide. The company should have done this as well. I also dropped out reports that were not serious since including these can make it difficult to appreciate serious risks.

[1] See Ex. 5206 (reference March 15, 2001).
[2] See Deposition of Manfred Hauben (30(b)6 Pharmacovigilance) July 2007.

Exhibit 4147

This is a chart that Plaintiff's counsel prepared at my request. The data are from the Defendants' own database. The database was given to the Plaintiffs lawyers and made available to me. So what you are looking at here is simply a chart of the data that Defendants had in 2002, before Mr. Smith died. Here are the figures that you can see for yourself:

Overdoses is at 7.23%
Depressive Disorders is at 3.22%
Behavior and socialization disturbances are at 1.98%
Suicidal and Self Injurious Behavior is at 1.86%

36. When you look at these data in a comprehensive manner as Pfizer should also have done, there are several events of concern that come to the forefront, particularly depression and suicidal behavior.

Exhibit 2061

37. In 2006, unfortunately already after Mr. Smith died, the company developed another signal detection plan: a "Gabapentin Data Capture Aid". My point in showing you this document is that Defendants should have and could have come up with this plan, years before Mr. Smith died. This exhibit is important because it shows the Defendants knew it was feasible to look specifically at suicide related events. There is no reason why this plan was delayed until 2006. It should have been implemented in 1994 when the drug was first put on the market and Defendants already knew that there were concerns with depression and suicide attemps associated with Neurontin.

Look at the side effect terms (at page 3) in this exhibit that Defendants were going to review: "Potentially suicide/self-injury related adverse events". There are then 10 additional adverse events listed there. This shows that the company agrees that it was appropriate to combine the suicide related terms, just as I did a few moments ago.

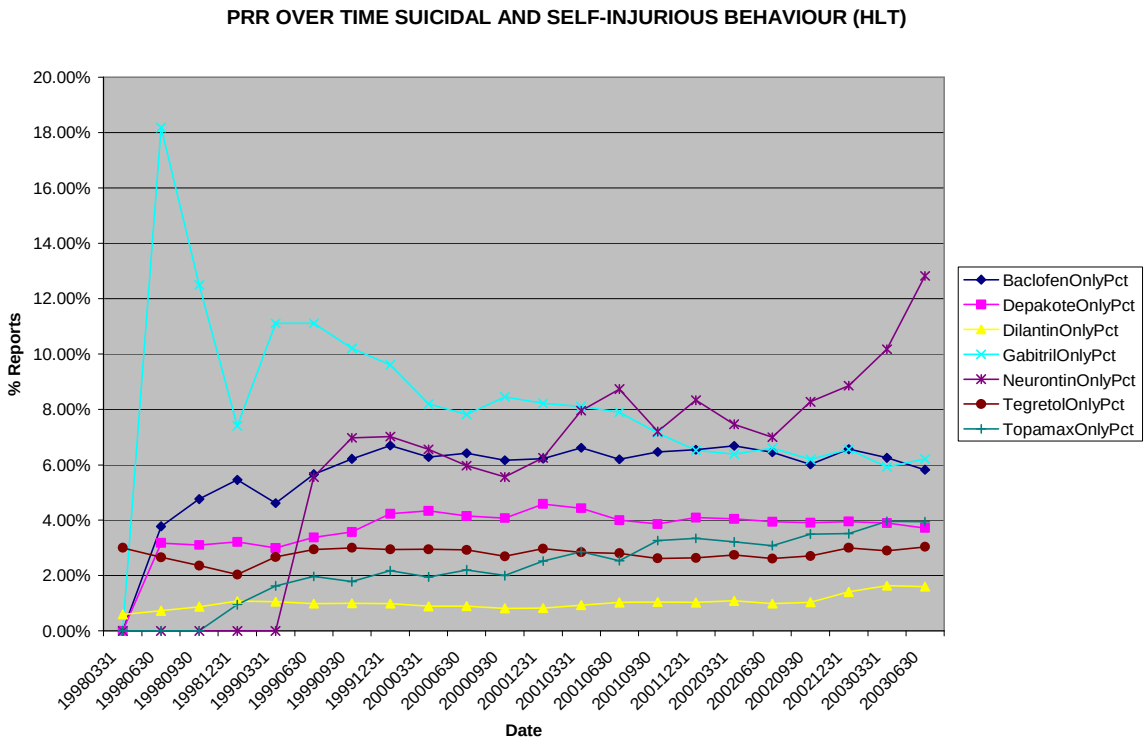
What's my point? My point is that if Defendants would have not delayed until 2006 to compile their "Data Capture Aid", they would have known about this safety signal no later than 2002 and before Mr. Smith died.

Pfizer failed to warn

Proportional Reporting Ratio (PRR) of Adverse Events

38. I have also addressed a presentation called the Proportional Reporting Ratio (a "PRR"). This presentation allows me to compare the strength of the signal for suicidality with Neurontin against the strength of the signal with other similar epilepsy drugs. The safety signal for Neurontin should have resulted in a warning by Defendants to doctors and patients.

39. Take a look at this chart, titled "PRR" Over Time Suicidal and Self-Injurious Behavior (HLT)". In this chart we see that Neurontin, Gabitril, and Baclofen are at or near the top of the grouping. Neurontin and Gabitril have similarities and are both used heavily off-label for similar conditions. The three drugs together are known to have common effects relating to GABA, one of the brain neurotransmitters we talked about earlier.



40. All three of these drugs appear to have the highest percentages of suicidal and self injurious events over a period of years. No later than mid 2001, Defendants had a safety signal of a possible association between Neurontin and suicidal effects. Specifically, the percentage of reports regarding serious events with Neurontin, Gabitril and Baclofen are approximately twice as high as the percentages of reports associated with the other anti-epileptic drugs used to treat similar conditions.

41. Look at the chart to see that Neurontin's % becomes the highest of the group beginning with 2001. PRR assessments (visually or mathematically derived) are common approaches

for evaluating safety signals. I prefer to show all the percentages (instead of limited ratios) because it provides more information and can make it easier to see multiple relationships. It is important to realize these charts do not establish causation. They show signals that the company, if it is doing its job, will look for and investigate. Based upon my review of the information provided by the company, at no time before Mr. Smith died, did the company compile and/or share these types of data. This falls below what a drug company should be doing when monitoring the safety of a drug, especially one that is used mostly in off label populations.

Exhibit 5791

42. Now, I must also tell you that Pfizer did its own calculation of reports relating to suicide related events. Unfortunately for Mr. Smith, the company only did this because FDA required the company to review the information. This chart was created at a time that the company was already aware that the FDA had concluded that Neurontin and other drugs increased the risk of sucidal behavior. Their analysis showed a safety signal for suicidality. You can see a huge increase in the percentage of suicide related events reported with Neurontin use through 2002, before Mr. Smith died. What's also important about this chart is that the company combined various terms related to suicide just as I have done. They also looked at the percentage of reports at various points in time similar to the way I have done.

Exhibit 4159
Blume Declaration, April 2008
Altman-B

43. Using Defendants' own confidential data that was provided to Plaintiffs' counsel and then made available to me, I asked Plaintiffs' attorneys to make the chart with Defendants' data. You can see that our chart is similar to Pfizer's chart --- you can see a dramatic increase in the percent of completed suicides before Mr. Smith's death in 2004. This was a safety signal that should have spurred Defendants to act and warn doctors and patients.

Exhibit 4159
Blume Declaration, April 2008
Altman-D

44. I also compared the percentage of suicide-related events with Neurontin to all other drugs for which data was available. Take a look at this exhibit. You can see that the percentage of reports for Neurontin was higher than all other examined drugs for years before Mr. Smith died in 2004. You can see that the plot line for Neurontin hovers at about 3 %, while all other drugs are lower at 1 %. The safety signal was significant by 1999. What this means is that by itself, even if the company knew nothing else about Neurontin, the company should have taken actions to figure out what was going on. Had they looked in their own clinical trial data and what the FDA had said when the drug was first approved, they would have

realized that there was a serious risk of suicidal behavior that was not adequately disclosed to doctors and patients.

45. Taking the percentage charts above, this was more than enough information for the company to realize that 1) sucide was not adequately labeled and 2) cause the company to perform an extensive review of the existing data. In effect, I did that review in reaching these opinons. To the best of my knowledge, to date, no Defendant employee or Defendant expert has ever performed such a systematic review of the information. This review included the literature, the clinical trial data, and the post marketing safety information.

46. Now, Defendants may say that the words "suicidal" or "suicide gesture" were included in the premarketing labeling events for Neurontin, but this was only in their laundry list of side effects. This was simply not good enough in terms of adequately providing doctors and patients with directions to use Neurontin safely, particularly in light of the postmarketing evidence I have shown you today.

47. It is also important that until after Mr. Smith died, the company did not warn doctors that Neurontin was associated with the risk of "completed" suicide. There was some language that the company buried in the label that said "suicidal" and "sucide gesture". Neither one of these terms tell doctors about the risk. Even Pfizer itself was telling the FDA that "completed" suicide was not a term warned about in their label. Until after Mr. Smith died, whenever the company received a completed suicide report, they sent it in to the FDA as an unexpected, unlabeled side effect. There is no way that the label could have been telling doctors of the risk of actual "completed" suicide if the company was telling the FDA it wasn't in the label in the first place.

EXHIBIT 2195

48. In 2006, the FDA wrote to the company requesting that the label be changed with respect to suicide and related events. As far as the FDA was cocnerned, the existing terms were unclear. When the label was finally changed, after Mr. Smith died, the FDA asked the company to ADD sucide to the label which the company agreed to do. So, don't believe the defendants if they claim that they ever warned for "suicide" during Mr. Smith's life. If "suicide" was already in the label, then Pfizer would not have had to add the term after Mr. Smith was dead.

49. Furthermore, it is routine that drug companies update their labels based upon only post marketing adverse event reports. Here, Defendants had far more information and failed to make the appropriate changes.

Exhibit 2001

50. In fact, Defendant Warner Lambert pled guilty to illegally promoting Neurontin for off-label uses, and as part of this admission of guilt, they admitted that Neurontin had "inadequate directions for use." Why is this important to my opinion on how Defendants failed to warn about suicide related events? Well, "directions for use" include informing the

doctors and patients about how to use Neurontin safely, and Defendants did not have adequate directions for use regarding risks of suicide-related events. So, patients and doctors were not informed to use Neurontin safely.

51. The Defendants may tell you that until the FDA in 2008 warned doctors about risks of suicidality, they had no idea about Neurontin and suicide. Well, the facts I have showed you today clearly indicate that their argument is not true. While Defendants didn't have the FDA's analysis until 2008, they knew of all these things I have told you about today, and all of those things should have led to an enhanced warning to doctors about the potential for suicide related side effects with Neurontin. They did not need FDA's epidemiology study across all epilepsy drugs to warn people about their specific drug product. As I explained earlier, the drug company did not need definitive proof that Neurontin causes suicidality to enhance their labeling and warn doctors and patients about the potential for suicidal behavior with Neurontin.

Lets take a look at the FDA's meta-analysis review of epilepsy drugs, which included Neurontin.

Neurontin increases the risk of suicidal behavior

Exhibit 3849
U.S. FDA Alert on Anticonvulsants and Suicidality

52. Lets look at Exhibit 3849. In January 2008, the FDA issued a safety alert after reviewing and analyzing clinical trials from 11 anti-convulsant drugs, including Gabapentin (its brand name being Neurontin). The FDA analysis indicated that "Patients taking antiepileptic drugs had approximately twice the risk of suicidal behavior or ideation compared to patients receiving a placebo." This analysis allows the FDA to review 11 similar drugs to determine if there is a common result that can be applied to all the drugs (and all uses) in the analysis. Neurontin was one of the 11 drugs in the analysis.

Exhibit 2808
FDA Statistical Review & Evaluation 2008

53. In addition to the nationwide FDA Alert, the FDA made public its Statistical Review and Evaluation of the meta-analysis. In its conclusion, the FDA said the following:

> "In conclusion, antiepileptic drugs are associated with increased risk of suicidality relative to placebo in randomized placebo controlled trials. The effect appears consistent among the group of 11 drugs."
>
> So, this means that Neurontin, as one of the drugs in the meta-analysis, is considered by the FDA to be associated with an increased risk of suicidality.

54. Pfizer disagrees with the FDA's findings that Neurontin is associated with suicidality. To respond to the FDA's results, the company prepared a report that they presented to the FDA. The FDA reviewed the document and gave the company the opportunity to explain its position at a public hearing in July 2008. After reviewing Pfizer's materials and presentation, the FDA specifically rejected the company's position with respect to Neurontin. What is interesting is that Christopher Wohlberg, the Pfizer executive who spoke at the FDA hearing defending Neurontin, thought very differently about the drug 10 years earlier.

EXHIBIT 5800

55. This is a document from 1999 that predates Pfizer purchasing Warner-Lambert. In contrast to the defense noted above, Christopher Wohlberg describes Neurontin as the "snake oil of the 20th century".

EXHIBIT 2015:
Audio/Video FDA Advisory Hearing

56. We even have video of the FDA advisory committee hearing from July 2008, where Dr. Russel Katz from the FDA, explained that the FDA's meta-analysis of the drugs was proof of causation for all the drugs, including Neurontin.

EXHIBIT 5809

57. Even in March of 2009, the company continued its efforts to deny that Neurontin increases the risk of suicide. For the pending labeling change that was completed in April, 2009, the company wanted the warning to say "may increase the risk of suicide". Dr. Russel Katz, a leading regulator at the FDA rejected that statement and again stated that the agency believed that all of the drugs in the alert increase the risk of suicide.

58. Besides Pfizer's own report which was specificially rejected by the FDA, Defendants undertook other efforts to defend Neurontin. Defendants' expert, Robert Gibbons, published an article in the Archives of General Psychiatry in 2009, and noted he did not find an increased risk of suicide attempts in patients with bipolar disorder who took anticonvulsants.

59. However, other authors who are not hired by Defendants have done studies after the FDA analysis and they have drawn conlusions similar to the FDA. I have reviewed and considered these articles, which were just published in March and April 2010. Their conclusions are consistent with my own opinions regarding Neurontin.

Exhibit: Olesen et al.,
Antiepileptic drugs and risk of suicide: a nationwide study
in Pharmacoepidemiology and Drug Safety (March 2010)

60. In March 2010, the Journal of Pharmaco-epidemiology and Drug Safety published a study titled, "Antiepileptic drugs and risk of suicide: a nationwide study". The authors studied a population group of 169,725 patients. There were identified 52,203 Gabapentin patients. The authors stated (at page 4) that the result of their study "showed a trend towards lowered risk associated with the usage of carbamazepine and an increased risk with the usage of gabapentin."

Exhibit:
Patorno, E., et al.,
Anticonvulsant Medication and the Risk of Suicide, Attempted Suicide, or Violent Death,
JAMA (April 14, 2010)

61. In April 2010, the Journal of American Medical Association published an article titled, "Anticonvulsant Medication and the Risk of Suicide, Attempted Suicide, or Violent Death". The authors had an "objective": These authors set out "to evaluate the risk of suicidal acts and combined suicidal acts or violent death associated with individual anticonvulsants."

These authors (at page 1406) found that "the risk of attempted or completed suicide was meaningfully increased for gabapentin. They do indicate that there is "no clear understanding of a mechanism of action that could lead to suicidal behavior," but then they go ahead and say that Gabapentin has been "associated with behavioral problems such as aggression and hyperactivity…"

So, what does this article teach us? These epidemiology statistics regarding Gabapentin confirmed there is scientific, reliable evidence that is consistent with my opinion that Gabapentin can cause depression and suicidal behavior.

62. In conclusion, my opinion in this lawsuit is given to you with a reasonable degree of scientific certainty that Gabapentin can cause depression and suicidality in people who take this drug. It is also my opinion that that there were sufficient numbers of suicide-related side effects regarding neurontin to warrant a change in the Defendants' labeling for Neurontin before Mr. Smith died on May 13, 2004. Defendants' failure to include a prominent, enhanced warning related to suicide events means that doctors and patients did not have adequate risk-benefit information about Neurontin. Defendants also failed to include warning information in their advertisements, letters to doctors, and their own sales representatives did not share this information with doctors when they would visit their offices.

63. In this statement, I have summarized my opinions and the bases for the opinions, and I have detailed for you the areas that Mr. Lanier told you about in his opening statement, including the following areas:

A.Only FDA approved uses can be advertised.

B. Neurontin is an epilepsy drug.
C. Neurontin is only approved for limited pain use.
D. Neurontin was never approved for Richard Smith's type of pain: general neuropathic pain.
E. Neurontin has significant effects.
F. Neurontin increases the risk of suicide.
G. Pfizer ignored red flags.
H. Pfizer failed to warn.

Thank you for your time, and to the extent that counsel, the court, or the jury has questions, I am of course available to address them.